

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/802,220

Confirmation No. 3562

Applicant: Uemoto

Filed: March 17, 2004

TC/AU: 1628

Examiner: Pagonakis, A.

Docket No.: 227833

Customer No.: 23460

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 C.F.R. § 1.131 OF
YOSHIFUMI UEMOTO**

Sir:

I, Yoshifumi Uemoto, do hereby declare:

1. I am the inventor of the subject matter disclosed and claimed in the above-identified patent application ("the present invention").
2. A pharmaceutical composition comprising (i) a cholesteryl ester transfer protein inhibitor that is *S*-[2-([1-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methylpropanethioate (JTT-705) and (ii) crospovidone was conceived of and reduced to practice prior to June 21, 2001. Further, a pharmaceutical composition comprising (i) a substantially crystalline cholesteryl ester transfer protein inhibitor that is JTT-705, in which the amount of inhibitor in amorphous form does not exceed about 10% and (ii) a water-insoluble concentration-enhancing additive was conceived of and reduced to practice prior to June 21, 2001.
3. As merely an example of both the conception and reduction to practice of these compositions, Exhibits A and B are attached to this Declaration.

4. Exhibits A and B are true and accurate copies of documents prepared before June 21, 2001. Dates and information irrelevant to the purposes of this Declaration have been redacted from Exhibits A and B as attached hereto.

5. Exhibits A and B report on the preparation of pharmaceutical compositions comprising (i) JTT-705 and (ii) crospovidone. In particular, Exhibit A reports on the preparation of a 100 mg dosage tablet comprising 100.000 mg JTT-705 (cholesteryl ester transfer protein inhibitor), a sufficient quantity¹ of crospovidone (water-insoluble concentration-enhancing additive), 6.000 mg hydroxypropylmethyl cellulose 2910 (binder), 116.747 mg lactose (diluent), 175.120 mg microcrystalline cellulose (diluent), 90.000 mg low substituted hydroxypropyl cellulose (disintegrant), 18.000 mg talc (lubricant), and 1.200 mg magnesium stearate (lubricant). Similarly, Exhibit B reports on the preparation of a 300 mg dosage tablet comprising 300.000 mg JTT-705 (cholesteryl ester transfer protein inhibitor), a sufficient quantity¹ of crospovidone (water-insoluble concentration-enhancing additive), 18.000 mg hydroxypropylmethyl cellulose 2910 (binder), 90.000 mg low substituted hydroxypropyl cellulose (disintegrant), 18.000 mg talc (lubricant), and 1.200 mg magnesium stearate (lubricant). The JTT-705 used in the pharmaceutical compositions described in Exhibits A and B was crystalline. The weight ratio of the JTT-705 (cholesteryl ester transfer protein inhibitor) to the crospovidone (water-insoluble concentration-enhancing additive) in both the 100 mg and 300 mg dosage tables was about 2.5:1. These tablets are the 100 mg and 300 mg dosage tablets described in Examples of the above-identified patent application (see especially Example 1, paragraphs 0118 and 0119).

6. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: March 28, 2011

Yoshifumi Uemoto
Yoshifumi Uemoto

¹ Sufficient quantity is calculated as follows:

(Granulation weight) – (JTT-705 API weight) – (hydroxypropylmethyl cellulose 2910 weight) = (weight of crospovidone)

EXHIBIT A

日本たばこ産業株式会社

医薬総合研究所 製剤研究所

作成・作業者	承認・製造管理責任者
 REDACTED	 REDACTED

治験薬製造指図書・製造記録書

品名	JTT-705錠 100mg	製品標準書番号	REDACTED
ロット番号	REDACTED	包装要領書番号	REDACTED
パッチサイズ	REDACTED	製造指図書番号	REDACTED
製造年月日	REDACTED	製造依頼年月日	REDACTED
		製造依頼番号	REDACTED
		使用目的	REDACTED

原料名	製造業者	ロット番号	処方量MG/T	標準的仕込量G/B
JTT-705原薬	日本たばこ産業㈱	K	100.000	450.0
クロスポビドン	BASF	04-9180	適量	適量
ヒト・キシブ・ロビ・メチルセルロース2910	信越化学㈱	901041	6.000	27.0
造粒末	—	—	145.933	656.7
乳糖 (ダイラクトース'R)	カイクト産業(株)	990111	116.747	525.4
結晶セルロース	旭化成工業(株)	28B1	175.120	788.0
低置換度ヒト・キシブ・ロビ・メチルセルロース	信越化学㈱	805222	90.000	405.0
タルク	松村産業㈱	0224	18.000	81.0
ステアリン酸マグネシウム	太平化学産業㈱	98122101	1.200	5.4
計	—	—	547.000	2461.5

包装仕様	REDACTED
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保存条件	REDACTED
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ラベル見本	出来高明細
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REDACTED	REDACTED
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備考

		Japan Tobacco, Inc. Central Pharmaceutical Research Institute, Pharmaceutical Development Laboratories			
Manufacturing instruction and record for investigational drug product		Persons in charge of preparation procedures, Seals of Uemoto and Hirahara, REDACTED	Approved by manager of manufacturing control, Seal of Sumani, REDACTED		
Product name	JTT-705 tablet, 100 mg		No. of product master formula		
Lot No.	REDACTED		No. of packaging procedure		
Batch size	REDACTED		No. of manufacturing instruction		
Manufacturing date	REDACTED		The date of manufacturing order		
			No. of manufacturing order		
			REDACTED		
			REDACTED		
Components and composition (theoretical quantities)					
Raw material name	Manufacturer	Lot No.	Weight per tablet MG/T	Amount per batch G/B	
JTT-705 API	Japan Tobacco, Inc.	K	100.000	450.0	
Crospovidone	BASF	04-9180	Sufficient quantity	Sufficient quantity	
Hydroxypropyl methylcellulose 2910	Shinetsu Chemical	901041	6.000	27.0	
Granulation weight	—	—	145.933	656.7	
Lactose (Dilactose R)	Froint Industry	990111	116.747	525.4	
Microcrystalline cellulose	Asahi Chemical	28B1	175.120	788.0	
Low substituted hydroxypropylcellulose	Shinetsu Chemical	805222	90.000	405.0	
Talc	Matsumura Industry	0224	18.000	81.0	
Magnesium stearate	Taihei Chemical Industry	98122101	1.200	5.4	
Total weight			547.000	2461.5	
Packing specification		REDACTED			
Storage condition		REDACTED			

Description	Production results, detailed	
REDACTED	REDACTED	
Note	REDACTED	

EXHIBIT B

日本たばこ産業株式会社

医薬総合研究所 製剤研究所

作成・作業者	承認・製造管理責任者
	 

治験薬製造指図書・製造記録書

品名	JTT-705錠 300mg	製品標準書番号	REDACTED
ロット番号	REDACTED	包装要領書番号	REDACTED
パッチサイズ	REDACTED	製造指図書番号	REDACTED
パッチ数	REDACTED	製造依頼年月日	REDACTED
製造年月日	REDACTED	製造依頼番号	REDACTED
		使用目的	REDACTED

原料名	製造業者	ロット番号	処方量MG/T	標準的仕込み量G/錠	総仕込み量G/TOT.
JTT-705原薬	日本たばこ産業㈱	K	300.000	600.0	3000.0
クロスボビドン	BASF	04-9180	適量	適量	適量
ヒト"ヨシフ"ロビ"ルメチルセロース2910	信越化学㈱	901041	18.000	36.0	180.0
造粒剤			437.800	875.6	4378.0
低密度ヒト"ヨシフ"ロビ"ルセロース	信越化学㈱	805222	90.000	180.0	900.0
タルク	松村産業㈱	0224	18.000	36.0	180.0
ステアリン酸マグネシウム	太平化学産業㈱	98122101	1.200	2.4	12.0
計			547.000	1094.0	5470.0

包装仕様

REDACTED

保存条件

REDACTED

ラベル見本

出来高明細

REDACTED

REDACTED

備考

		Japan Tobacco, Inc. Central Pharmaceutical Research Institute, Pharmaceutical Development Laboratories			
Manufacturing instruction and record for investigational drug product		Persons in charge of preparation procedures, Seals of Uemoto and Hirahara, REDACTED	Approved by manager of manufacturing control, Seal of Suman, REDACTED		
Product name	JT-705 tablet, 300 mg		No. of product master formula	REDACTED	
Lot No.	REDACTED		No. of packaging procedure	REDACTED	
Batch size	REDACTED		No. of manufacturing instruction	REDACTED	
Number of batches	REDACTED		The date of manufacturing order	REDACTED	
Manufacturing date	REDACTED		No. of manufacturing order	REDACTED	
		REDACTED	Intended usage purpose	REDACTED	
Components and composition (theoretical quantities)					
Raw material name	Manufacturer	Lot No.	Weight per tablet MG/T	Amount per batch G/B	Total amount G/Tot.
JT-705 API	Japan Tobacco, Inc.	K	300.000	600.0	3000.0
Crospovidone	BASF	04-9180	Sufficient quantity	Sufficient quantity	Sufficient quantity
Hydroxypropyl methylcellulose 2910	Shinetsu Chemical	901041	18.000	36.0	180.0
Granulation weight	—	—	437.800	875.6	4378.0
Low substituted hydroxypropylcellulose	Shinetsu Chemical	805222	90.000	180.0	900.0
Talc	Matsumura Industry	0224	18.000	36.0	180.0
Magnesium stearate	Taihei Chemical Industry	98122101	1.200	2.4	12.0
Total weight	—	—	547.000	1094.0	5470.0
Packing specification REDACTED					
Storage condition REDACTED					
Description REDACTED		Detailed production results REDACTED			

Note